Exhibit B

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION **THIS DOCUMENT RELATES TO WAVE 1 TVT CASES**	**Master File No. 2:12-MD-02327** **MDL 2327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**

EXPERT REPORT OF JOSEPH CARBONE, M.D.

1. BACKGROUND AND QUALIFICATIONS

I am Board Certified in Urology and Female Pelvic Medicine and Reconstructive Surgery. I have been Medical Director of the Piedmont Institute of Continence and Urinary Control for 15 years. I began my medical training when I was accepted into the Washington University in St. Louis Scholars Program in Medicine as one of ten students selected in the country from high school into the Washington University in St. Louis School of Medicine. Upon completion of my undergraduate degrees in Biochemistry and Philosophy, I completed training at the Washington University in St. Louis School of Medicine that has consistently been ranked as one of the top ten medical schools in the country. I was accepted into the Urology residency program there, which at the time was ranked as one of the top five programs in the country. In addition to studying prostate cancer surgery under Dr. William J. Catalona and endourologic surgery under Dr. Ralph V. Clayman, I participated with Dr. Carl G. Klutke in

some of the earliest experiences in the use of transvaginal mesh for the treatment of stress urinary incontinence in the United States. I personally met and discussed the technique with the late Dr. Ulf Ulmsten who has been credited with the original research on the suburethral transvaginal tension-free mesh in Europe. After completing my residency training, I was selected as one of two residents in the world into the UCLA fellowship in Neurourology, Urodynamics and Female Urology under the tutelage of female pelvic reconstructive surgeon, Dr. Shlomo Raz.

After training, I elected to pursue a career in a small-town private practice where those in need could get the greatest benefit from my training. It is there where I established the Piedmont Institute for Continence and Urinary Control and brought world-class care to a rural setting. I have maintained my skills through the performance of hundreds of suburethral mesh slings. I have kept abreast of the improvement in delivery techniques and have performed every iteration of the TVT including the original retropubic TVT, the transobturator TVT, the single incision TVT, the TVT Exact and the TVT Abbrevo.

I have shared my knowledge and training with the surgical community through my participation in the Ethicon preceptorship program. Through the years, I have provided education and training to hundreds of surgeons in the techniques of incontinence surgery using the retropubic, obturator, and single incision slings. As I always explained at my presentations, the purpose of the training was to ensure the proper performance of the various techniques so that everyone could expect relatively uniform risks and outcomes rather than persuade

anyone to adopt the techniques. I felt strongly and always stressed that choice of what surgery to perform was a decision between the surgeon and the patient based on a balance between the most recent and reliable scientific data available in the peer-reviewed literature and the patient's own personal opinions. The purpose of the preceptorship was to provide the surgeon with hands-on training or real-life experience with the technique of interest, while providing information on device usage, risks and complication avoidance and management. However, the most important step in the selection of the patient and technique for performing incontinence surgery has been and will always be the clear and direct communication between the physician and patient through the objective process of informed consent.

2. INFORMED CONSENT

Informed consent is the process by which the treating health care provider discloses appropriate information to a competent patient so that the patient may make a voluntary choice to accept or refuse treatment.[1] It originates from the legal and ethical right the patient has to direct what happens to her body and from the ethical duty of the physician to involve the patient in her health care. First and foremost, accurate, adequate and relevant information must be provided truthfully in a form and language that the patient can understand. This is the primary responsibility of the physician. It is the reason why we read peer-reviewed journals, attend CME conferences and keep our Specialty Certifications up-to-date. It is also the reason why the TVT IFUs always recommend training on the use of the various incontinence surgery systems. On the other hand, while the

information provided to a patient should include all material risks, the list of risks and side effects cannot be exhaustive to the level of absurdity and impracticality.[2] What is expected is that the doctor should provide information that a prudent or reasonable patient would expect to make a knowledgeable decision about the course of action to be taken in the presence of alternatives.

What one must recognize, however, is that all interventions, including incontinence surgery, carry risk. This is the primary responsibility of the patient. Patients' perception of risk of a medical intervention is highly individualistic, variable and unpredictable. It is an element known only to the patient and must be respected by the physician. Patient should be given opportunity to ask questions and clarify all doubts. Similarly, patients have the responsibility to address these concerns either with their physician or another health care provider before acknowledging informed consent.

Only when both responsibilities are met can the process of informed consent be considered complete. This creates the setting in which a successful intervention for incontinence can be accomplished regardless of alternative chosen.

3. DIAGNOSIS

Stress urinary incontinence (SUI) is a symptom, a clinical sign, and a urodynamic observation. The symptom of SUI is best defined by the International Continence Society (ICS) as "involuntary leakage of urine on exertion, effort, coughing, or sneezing."[3] SUI is the most commonly diagnosed subtype of incontinence in adult women. The majority of published data suggest

that around 50% of incontinence women will exhibit pure SUI with a further 30% experiencing mixed incontinence.[4] Thus, potentially large numbers of adult women with troublesome urine leakage will have a "stress component" to their incontinence. In a review of population-based studies, a wide range in the prevalence of incontinence has been reported in the literature. The median prevalence of female urinary incontinence (UI) was 27.6% (range: 4.8-58.4%) and the prevalence of significant incontinence increased with age. Other risk factors included parity, obesity, chronic cough, depression poor health, other lower urinary tract symptoms, previous hysterectomy, and stroke.[5] Despite the well-documented negative effect on quality of life, a large pan-European questionnaire study found that less than one in three women with UI had consulted their doctor and that this pattern was reproducible across all countries with little variation.[6] It would seem therefore that despite the bothersome nature of their symptoms and the obvious effect on quality of life, the majority of women are disinclined to seek medical intervention perhaps in the belief that treatment will not be successful or that surgery for their condition is perceived as unacceptable.

The diagnosis of SUI is suggested from the clinical history; however recent reports have questioned the validity of this approach and recommend further investigations prior to making a diagnosis and considering treatment. In a retrospective review of over 6,000 women, a diagnosis of pure SUI could be made in only 5% of women based on history alone. Furthermore, around one in four women with a suggested diagnosis of SUI from the clinical history did not have

SUI diagnosed following urodynamic studies (UDS).[7] In a similar study of almost 3,500 women, a diagnosis of SUI based on clinical history can only be made in less than 10% of women. In addition, over 20% of those women were given alternative diagnoses following UDS.[8] These data highlight the high level of inaccuracy associated with clinical history and suggest further investigation is needed prior to recommending treatment for SUI.

According to the 2009 American Urologic Association (AUA) guidelines for female SUI, the sine-qua-non for a definitive diagnosis is the demonstration of involuntary urine loss from the urethral meatus coincident with increased abdominal pressure such as those occurring during coughing and straining.[9] On the basis of a focused history and physical examination with a comfortably full bladder, the AUA panel suggests that the diagnosis of SUI is fairly straightforward in the index patient. Nevertheless, they concede that certain comorbidities relating to coexisting conditions might affect the outcome of treatment and influence surgical technique and the specifics of patient counseling. These comorbidities include:

- urinary urgency and urge incontinence (diagnosed by history, questionnaire, bladder diary);
- anatomic features such as pelvic organ prolapse (diagnosed by history, exam); and/or
- the presence of detrusor overactivity, urethral obstruction, low bladder compliance and impaired or absent detrusor contractility (diagnosed by uroflow, postvoid residual volume, urodynamics).

The AUA panel recognizes that there are few facts and many opinions about predicting the outcome of surgery based on the comorbidities described above. The need for further evaluation of any given patient depends on a number of factors including the degree of certainty and comfort that the physician has about the diagnosis and the impact that further studies will have on the diagnosis, treatment options, treatment risks and likely outcomes. It is the physician's responsibility to thoroughly investigate and understand the patient's specific comorbidities to allow for individualized treatment planning, for informed consent and for the surgeon's estimate of a successful outcome and the potential occurrence of complications.

4. NON-SURGICAL TREATMENTS

The most conservative treatments for SUI include the non-surgical options. Behavioral changes such as weight loss, smoking cessation, limiting fluid intake and timed voiding to keep the bladder relatively empty are often first-line interventions. There is a paucity of literature regarding the success of these measures. In my experience, these interventions alone have limited success except for the patient with the most minimally bothersome symptoms. However, these conservative measures serve as useful adjuncts for any more invasive interventions considered.

Pelvic floor muscle exercises (Kegels) represent another non-surgical option for the treatment of SUI. The concept is to strengthen the pelvic floor supporting the bladder and urethra to provide a backboard of support during increases in abdominal pressure such as those occurring during coughing and

straining. In addition to increasing pelvic floor tone, the regular performance of Kegels exercises improves the ability for patients to consciously contract of the pelvic floor in anticipation of increases in abdominal pressure. Modifications of these exercises include the use of vaginal weights, physical therapists, electrical stimulation and/or biofeedback. As with behavioral modifications, pelvic floor muscle exercises alone have limited success except for the patient with the most minimally bothersome symptoms. Again, however, these conservative measures serve as useful adjuncts for any more invasive interventions considered.

Several intravaginal devices are designed to correct the problem of SUI. Incontinence pessaries provide either external support or compression of the urethra. They are usually used when SUI presents in combination with pelvic organ prolapse. Poise Impressa Bladder Supports is a vaginal tampon designed to create a transient urethral obstruction by placing pressure on the urethra. Women wear this disposable device when they want to avoid leakage and remove it in order to urinate.

As for pharmaceutical options, there are no FDA approved medications for SUI. Topical estrogen cream after menopause can be used for the treatment of postmenopausal atrophy; however, there are mixed opinions regarding its efficacy for urinary incontinence.

Finally, the use of transurethral bulking agents has been FDA approved for the treatment of SUI due to a deficiency of the urinary sphincter. While this procedure does not exactly fit under the category of non-surgical treatment, it is performed endoscopically and does not warrant any surgical incision. The

concept is to augment the urethral mucosa to cause urethral coaptation and an improved seal mechanism to provide continence. There have been several materials on the market, including bovine collagen, autologous fat, calcium hydroxyapatite (Coaptite), carbon beads (Durasphere) and polydimethylsiloxane (Macroplastique). The success rate for this procedure is low and often requires multiple treatment sessions.

Overall, it can be summarized that while the non-surgical options for the treatment of SUI typically has limited success except for the patient with the most minimally bothersome symptoms, any one of them may be ideal for the patient with significant comorbilities that is not a good candidate for more invasive interventions. Again, it is the physician's responsibility to thoroughly investigate and understand the patient's specific comorbidities to allow for individualized treatment planning, for informed consent and for the surgeon's estimate of a successful outcome and the potential occurrence of complications.

5. KELLY PLICATION

The first surgical technique for female SUI that became a routine clinical procedure was initiated by the uro-gyencologist Howard A. Kelly (1858-1943) from Baltimore in 1900. Much like the transurethral bulking agents, the concept was to cause urethral coaptation and an improved seal mechanism to provide continence. Rather than augmenting the urethral mucosa; however, the Kelly plication compressed the urethra externally. It consisted of anterior colporraphy and plication of the bladder neck with deep mattress sutures. Continence was achieved through compression of the bladder neck and apposition of the urethral

walls. In 1914, Kelly presented the first detailed analysis and follow-up of twenty patients,[10] a milestone in the history of urogynecology and the standard of care for the next 60 years.

6. SUSPENSION PROCEDURES / TRANSMISSION OF PRESSURES THEORY

With the development of sophisticated manometric measurements in World War II, these instruments were soon utilized in the investigations of SUI. In the late 1940s, Enhorning developed a urethral catheter with two pressure transducers 5 cm apart, which permitted simultaneous measurement of vesicle and urethral pressures. Using this apparatus, he showed that, in continent subjects, urethral pressure exceeded vesical pressure, both at rest and during increases in intra-abdominal pressure. He hypothesized that this equal rise in vesical and urethral pressure was due to transmission of intra-abdominal pressure to the bladder and the part of the proximal urethra above the pelvic floor. In patients with SUI, there was deterioration of the intra-abdominal pressure transmission to the proximal urethra because it had dropped out of its anatomic position above the pelvic floor.[11] This became commonly known as the Transmission of Pressures Theory. Thus, the surgical mantra for any operation used to treat SUI after World War II was that, to be successful, the operation must result in the "high, fixed retropubic position" of the proximal urethra. It was believed that the mechanism of action of surgical treatment of SUI was the correction of the anatomic defect that permitted unequal intra-abdominal pressure transmission to the bladder versus the proximal urethra, namely urethral hypermobility.

Cystourethropexy was introduced by V. F. Marshall, A. A. Marchetti and K. E. Krantz in 1949.[12] The original operation involved an incision in the lower abdomen to expose the bladder neck and urethra. Permanent stitches such as Prolene were placed in the tissues near the bladder neck and proximal urethra, which were then lifted and tied to the tissue (fascia) behind the pubic bone or to the pubic bone itself. According to the dogma of the day, this pulled the urethra into a "high, fixed retropubic position" thus correcting urethral hypermobility and achieving urinary continence.

Colposuspension was introduced by J. C. Burch in 1961.[13] Again, an incision was made in the lower abdomen to expose the bladder neck and proximal urethra. Permanent sutures such as Prolene were placed in the anterior vaginal wall at the level of the bladder neck and proximal urethra and then sutured to the Cooper's ligament. Again, this pulled the urethra into a "high, fixed retropubic position" correcting urethral hypermobility and SUI.

Both the MMK and Burch procedures represent invasive techniques, requiring an abdominal incision, extensive intraoperative dissection and prolonged convalescence. The MMK fell out of favor because it had high bony complications and inferior long-term efficacy.[14] The Burch showed a similar drop off in long-term success rates. In the Kjolhede long-term study on Burch procedures, subjectively significant urinary incontinence was experienced by 56% of the patients.[15] In the Alcalay study, the Burch demonstrated further decline in cure rates, with only 19% of patients reporting no incontinence episodes.[16] In addition, the Burch procedure was associated with late complications in 220

women, including rectocele (32), cystocele (18), enterocele (35), dyspareunia (6), and groin or suprapubic pain (15).[17]

To minimize the morbidity associated with the open surgical suspension, A. J. Pereyra inaugurated vaginal needle suspension in 1959.[18] The operation involved dissection and exposure of the bladder neck and proximal urethra through the pelvic floor via a transvaginal approach. Permanent stitches such as Prolene were then affixed to the tissues near the bladder neck and proximal urethra and transferred using a "needle" from the vaginal incision, through the retropubic space to the abdominal fascia. Once the sutures were tied over the abdominal fascia, the proximal urethra was again pulled into a "high, fixed retropubic position" correcting urethral hypermobility and thus SUI.

This needle suspension technique became very popular with surgeons and patients alike because it did not require an abdominal incision, extensive intraoperative dissection or prolonged convalescence. Additional advantages include the ability to perform concomitant transvaginal procedures through a single incision/approach, optimization of operative exposure in obese patients, and facilitate surgery in circumstances in which the abdominal approach is contraindicated (eg: femoral-femoral vascular bypass graft, prior abdominoplasty, etc.). Multiple named modifications of the Pereyra vaginal needle suspension ensued including the Stamey procedure in 1973, the Raz procedure in 1981, and the Gittes procedure in 1987.

Unfortunately, despite the popularity of these procedures, the early failure rate proved to be quite high (>50% in some reports) and a Cochrane review

concluded that needle suspension surgeries had a lower subjective cure rate than the Burch culposuspension (74% v. 86%, respectively). Complications included detrusor instability, urinary tract infection, pelvic pain and dyspareunia.

7. TRADITIONAL SLING PROCEDURES

Sling surgery for SUI is actually a very old technique. The first method has historically been credited to Giordano in 1907 by using the gracilis muscle.[19] He detached a muscle from the thigh and translocated it retropubically as a sling around the urethra. Three years later R. Goebell performed a sling operation with the pyramidalis muscles in two girls.[20] He separated the muscles from the fascia and postulated an active muscular closure effect on the urethra. Paul Frangenheim used the same muscles together with the onlying fascia in 1914.[21] Walter Stoeckel suggested the combination of this muscle-fascia sling with a transvaginal muscular plication of the bladder neck (similar to a Kelly plication) in 1917.[22] This procedure was known as the Goebell-Frangenheim-Stoeckel operation in clinical terminology. In 1933, P. B. Price described the first sling utilizing rectus abdominus muscle.[23] In 1942, A. A. Aldridge described the first fascial sling.[24]

Contemporary pubovaginal sling surgery for SUI was introduced by McGuire in 1978.[25] The operation involved a low abdominal incision to the level of the rectus sheath. A long strip of rectus fascia was harvested. Dissection was then carried out vaginally to expose the bladder neck and proximal urethra. The fascial strip was then transferred under the urethra using a long clamp from the vaginal incision, through the retropubic space across the rectus musculature on

both sides. The sling ends were incorporated into the closure of the rectus sheath excision. Again, according to the dogma of the day, this pulled the proximal urethra into a "high, fixed retropubic position" thus correcting urethral hypermobility and achieving urinary continence. Modifications of this sling technique included the use of a retropubic sling made from different materials including the fascia from the outer thigh (fascia lata), sterilized and irradiated fascia from a cadaver donor (allograft), from an animal (xenograft), or synthetic materials.

Overall, the success rate of the traditional pubovaginal sling (PVS) techniques was good, but again was seen to decline over time. In the SISTEr trial at seven years, the urinary continence rate (no reported leakage by the patient) was only 13% for the Burch procedure and 27% in the pubovaginal sling group.[26] Also like the Burch procedure, the PVS can lead to significant complications including infection, pain, wound complications, sexual dysfunction and dyspareunia.

In addition, proper tensioning of the traditional PVS to achieve the optimal "high, fixed retropubic position" of the proximal urethra was exceedingly elusive. Commonly, traditional fascial slings placed under excessive tension caused compression of the urethra and blocked the flow of urine. This resulted in complications of urinary retention, incomplete bladder emptying, voiding dysfunction and de novo urgency. With synthetic slings, excessive tensioning could lead to erosion. Nevertheless, based on Enhorning's Transmission of Pressures Theory, surgeons were reluctant to completely abandon tensioning of

the sling for fear of not achieving successful high, fixed retropubic positioning of the proximal urethra in the treatment of SUI.

8. TENSION-FREE SLING PROCEDURES / INTEGRAL THEORY

In 1990, Drs. Ulmsten and Petros introduced the Integral Theory to replace Enhorning's Transmission of Pressures Theory as the accepted pathophysiologic etiology for SUI. The Integral Theory states that prolapse and most pelvic floor symptoms such as urinary stress incontinence, urgency, abnormal bowel or bladder emptying, and some forms of pelvic pain, mainly arise, for different reasons, from laxity in the vagina or its supporting ligaments, as a result of altered connective tissue.[27] The theory arose out of the research being done by Dr. Ulmsten and Petros to find a new way to treat SUI. They began to use several different types of meshes and placed them, tension-free, under the mid-urethra. This was a dramatic departure from the traditional mantra of the day, which dictated that successful incontinence surgery required tension on the proximal urethra and bladder neck to pull the urethra into a "high, fixed retropubic position."

The polypropylene mesh being used was not new to surgery. Polpropylene mesh had been used as a permanent human implant for decades prior. The first polypropylene meshes were developed and used by hernia surgeons in the 1950s. In the early 1970's, Ethicon developed Prolene mesh for hernia surgery. The Prolene mesh was made from the same material in Prolene sutures, which had been used since the 1960s. The Prolene sutures have been used for cardiovascular repairs, plastic surgery, hernia repairs and pelvic floor

repairs. Before its use by Dr. Ulmsten and Petros, the inflammatory response and appropriateness of Prolene in the body was well known.

Except a blue dye that was added for coloring, the original Prolene mesh used by Drs. Ulmsten and Petros was the same mesh that Ethicon has used in all its TVT products. It is a Type 1 macroporous monofilament mesh that has shown the best tolerability for use in stress urinary incontinence. Among the SUI meshes, it has the largest pore size, which allows for the natural infiltration by macrophages that reduces infection rates. In 2009, a Cochrane Review found that TVT mesh has better efficacy and lower erosion rates than multifilament non-Type 1 meshes.[28] Falconer also found minimal inflammation with the Prolene mesh and practically no tissue reaction even out to two years. There was no difference between paraurethral connective tissue in biopsies from patients operated on with Prolene tape and in controls two years after surgery.[29] No contraction was identified. In addition, the TVT mesh has the optimal weight and flexural rigidity for long lasting continence and tolerability. In a study to determine how the TVT mesh responds to stretch, increasing forces were applied and the mesh was tested for flexural rigidity and elongation.[30] At increasing forces, even beyond those found in vivo, there were no significant differences. This dispelled any concerns that there was fraying of the mechanically cut mesh that would cause a clinical effect in patients. In addition, with the addition of laser cut mesh in 2006 there was no difference found between the success and complication rates before and after the introduction of the laser cut mesh. Put simply, the Ethicon Prolene mesh, despite the addition of blue dye or different

cutting techniques, is appropriate for use in the body, and is both safe and efficacious as demonstrated by the literature.

By 1996, Dr. Ulmsten completed his first trial, which included 75 patients with two-year follow-up. Results revealed that 92% of the patients were cure or significantly improved, with no tape rejection, no defective healing, no intra-operative complications and no post-operative complications.[31] In 1997, Ethicon began to sell Tension-free Vaginal Tape (TVT) in Europe. In 1998, a prospective randomized study with six centers was carried out in Scandinavia and tested the safety and efficacy of the TVT device. A compilation of the date that was published in 1998 showed 915 cure rates, with another 7% significantly improved.[32] The results demonstrated the procedure was safe, effective and less invasive that prior anti-incontinence procedures. In addition, since the results of this multicenter trial were similar to those achieved by Dr. Ulmsten's single-surgeon experience, it revealed that the TVT had reproducible success. That is to say that less experienced surgeons were able to replicate the continence outcomes of experience surgeons without compromising patient safety.

In 1998, Ethicon began to sell TVT in the United States. The technique had become the most studied operation in the history of surgery for SUI and the results have been remarkably similar. In a 2008 randomized control trial comparing TVT versus Burch colposuspension with 5–year follow-up, the TVT had similar efficacy and patient satisfaction and less voiding dysfunction.[33] A 2009 Cochrane review of TVT versus Burch showed that TVT appeared to be as effective as open Burch colposuspension but with fewer complications, less

voiding dysfunction, shorter operative times, and higher safety.[34] These same findings were reproduced in a 2012 Cochrane Review as well.[35] Finally, a meta-analysis by Novara found that patient receiving midurethral tapes, particularly TVT, had a significantly higher overall and objective cure rates than those receiving Burch colposuspension.[36] Subsequent iterations of the original TVT product was made only in the surgical approach to minimize complications, not change efficacy.

The first evolution of the tension free sling came with the development of the obturator approach. Developed by Delorme as an "outside-in" approach and modified by DeLeval as an "inside-out" approach, the later became available in the US in 2004 as the Ethicon TVT-O sling. Obturator slings became popular because they intuitively reduced the risk of any pelvic injury (eg: bowel perforation, bladder perforation, major blood vessel trauma). By traversing a tract inferior to the pelvic floor, the needle was designed to stay out of the pelvis and away from bowel, bladder and major blood vessel. Nevertheless, by providing tension-free support at the mid-urethra, both the TVT-O and the TVT demonstrated effectiveness in the treatment of SUI. This is supported by the similar results achieved by both the TVT and TVT-O technique at 12 months, although there is a slight drop in the TVT-0 success rates at 24 months and 5 years.[37] [38] [39]

The next evolution of the tension-free sling came with the development of single incision slings. In 2006, Ethicon introduced the TVT Secur (TVT-S) device in response to feedback from surgeons who wanted an even less invasive

procedure to reduce potential complications. As a single incision sling, TVT-S required only one small vaginal incision and did not require separate incision for sling exit points. The TVT-S was designed to be placed in either a "U" approach (mimicking the TVT) or the "hammock" approach (mimicking the TVT-O). It utilized the same type Prolene mesh as the two prior techniques (TVT & TVT-O) but only introduced 8 cm of total mesh with the expectation that less mesh would cause less tissue reaction and complications. To secure the device to the fascia, the TVT-S had pieces of fleece made from Vicryl and PDS on each end to the mesh. As a single incision sling, substantial professional education was offered in connection with the device including Key Technical Points, cadaver labs, surgical videos and the opportunity for observation of and by experienced surgeons.

The latest evolution of the tension-free sling came with the abbreviated obturator approach. The TVT-A is identical to the TVT-O, utilizing the same trocars, the same route of placement and the same material, except instead of a full-length sling, the mesh is shorter and is not implanted into the adductor musculature at all. It promises the minimal complications of the single incision sling, with the reproducibility in placement of a TVT-O.

Regardless of the iteration of TVT device, all the Ethicon products share a number of commonalities. First, the Prolene mesh material is the same throughout all the products. The color may have changed and the edges may be laser or mechanically cut, but the fundamental characteristics of the Prolene mesh have remained the same. In addition, the products are all designed to be placed at the mid-urethra under no tension to follow the principles of the Integral Theory.

Implied in the name, the Ethicon products are all understood to be place in a tension-free manner, reducing the risk of urinary retention, incomplete bladder emptying, voiding dysfunction, de novo urgency and erosion.

9. TVT IFU

Instructions for use (IFU) accompany all medical devices like the TVT. An IFU is not intended to serve as a comprehensive guide for a surgeon. Instead, it provides information about the device, the procedure, the indications, and warnings and precautions that the surgeon can use in conjunction with his or her training and experience. A reasonably prudent surgeon will be trained in pelvic floor surgery, with or without mesh, before he or she attempts to implant a TVT. An IFU only supplements that training and experience.

The TVT IFU adequately warns of all risks and potential complications associated with the TVT. These risks are well known to the medical community. Even the FDA has acknowledged that that risks known to be common to pelvic floor surgery (even without mesh) include pain, infection, urinary problems, recurrent incontinence, pain during sexual intercourse (dyspareunia), bleeding, organ perforation, neuoro-muscular problems and vaginal scarring.[1]

The TVT IFU fairly and completely informs reasonably prudent surgeons about the TVT, including the procedure and the associated risks and potential complications.

[1] FDA, Considerations About Surgical Mesh for SUI, April 2, 2013. U.S. Food and Drug Administration http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/UroGynSurgicalMesh/ucm345219.htm downloaded Feb 10, 2016.

10. TVT PATIENT BROCHURES

Ethicon created patient brochures used to inform patients about TVT. A patient brochure does not replace the patient-surgeon relationship or the related informed consent process. TVT's patient brochures appropriately provide basic information to patients and recommend that she discuss her condition and options with her surgeon. Only a surgeon can determine, using his or her medical judgment, whether a particular patient is a candidate for TVT.

11. TVT PROFESSIONAL EDUCATION

Ethicon provides professional education to surgeons who desire such training. This professional education is not required for the purchase or implantation of TVT. Instead, Ethicon provides optional learning opportunities through didactic lectures, cadaver labs, and hands on training with experienced surgeons. This training is not intended to replace a surgeon's formal medical training and experience. Instead, it is intended to supplement it with relevant and up to date information about a particular device and procedure. Ethicon's TVT training is well planned, well executed, and goes beyond the industry standards for such training.

12. PROFESSIONAL ENDORSEMENTS

The American Urogynecologic Society (AUGS) is the largest professional society representing the medical specialty of urogynecology. The AUGS consists of more than 1,500 physicians. The AUGS has adopted a position statement that full-length mid-urethral slings such as the TVT (both retropubic and

transobturator) have been extensively study and are safe and effective relative to other treatment options.[40]

The Society of Urodynamics, Female pelvic medicine and Urogenital reconstruction (SUFU) represents the largest professional organization for urologists that is dedicated to improve the art and science of Urology through basic and applied clinical research in urodynamics and neurourology, voiding function and dysfunction, female urology and pelvic floor dysfunction. It is the oldest professional organization dedicated to this field. perform female pelvic medicine and reconstructive surgery. Both AUGS and SUFU have provided a position statement[41] in support of the use of transvaginal mesh for the surgical treatment in response to the July 2011 FDA white paper on the safety and effectiveness of transvaginal placement of surgical mesh specifically for pelvic organ prolapse. They wrote:

> *The polypropylene mesh midurethral sling is the recognized worldwide standard of care for the surgical treatment of stress urinary incontinence. The procedure is safe, effective, and has improved the quality of life for millions of women.*

In addition, they expressed concern regarding lawyers that have publicly advertised their services, targeting women with transvaginal mesh placed for both pelvic organ prolapse and stress urinary incontinence and the media that has reported on the pelvic organ prolapse mesh litigation. They wrote:

> *We are concerned that the multimedia attention has resulted in confusion, fear, and an unbalanced negative perception regarding the midurethral*

sling (MUS) as a treatment for SUI. This negative perception of the MUS is not shared by the medical community and the overwhelming majority of women who have been satisfied with their MUS.

Finally, they cite the FDA website[42] which, in 2013, stated clearly that: "The safety and effective of multi-incision slings is well-established in clinical trial that followed patients for up to one year.

13. CONCLUSION

The polypropylene (Prolene) midurethral sling has helped millions of women with SUI regain control of their lives by undergoing a simple outpatient procedure that allows them to return to daily life very quickly. With its acknowledged safety and efficacy, it has created an environment for a much larger number of women to have access to treatment. In the past, concerns over failure and invasiveness of surgery caused a substantial percent of incontinent women to live without treatment. One of the unintended consequences of this polypropylene mesh controversy has been to keep women from receiving any treatment for SUI. This procedure is probably the most important advancement in the treatment of stress urinary incontinence in the last 50 years and has the full support of both AUGS and SUFU, which are dedicated to improving the lives of women with urinary incontinence.

Dated: March 2, 2016

[1] Appelbaum PS. Assessment of patient's competence to consent to treatment. New England Journal of Medicine. 2007;357:1834

[2] KH Satyanarayana Rao. Informed Consent: An Ethical Obligation or Legal Compulsion? J Cutan Aesthet Surg. 2008;1(1):33

[3] Abrams P, et al. The standardization of terminology of lower urinary tract function. Neurourol Urodyn. 2002;21:167

[4] Irwin D, et al. Population-based survey of urinary incontinence, overactive bladder, and other lower urinary tract symptoms in five countries: results of the EPIC study. Eur Urol. 2006;50:1306

[5] Minassian VA, et al. Urinary incontinence as a worldwide problem. Int J Gynacol Obstet. 2003;82:327

[6] O'Donnell M, et al. Help-seeking behavior and associated factors among women with urinary incontinence in France, Germany, Spain and the United Kingdom. Eur Urol. 2005;47:385

[7] Agur W, et al. Could the National Institute for Health and Clinical Excellence guidelines on urodynamics in urinary incontinence put some women at risk of a bad outcome from stress incontinence surgery? BJU Int. 2009;103:635

[8] Digesu GA, et al. Do women with pure stress urinary incontinence need urodynamics? Urology. 2009;74:278

[9] Dmochowski RR, et al. Update of AUA guideline on the surgical management of female stress urinary incontinence. J Urol. 2010;183(5):1906

[10] Kelly HA, Dumm WM. Urinary inctoneintne in women, without manifest injury to the bladder. Surg Gynecol Obstet. 1914;18:444

[11] Enhorning G. Simultaneous recording of intravesical and intra-urethral pressure: a study on urethral closure in normal and stress incontinent women. Acta Chir Scand. 1961;276:1

[12] Marshall VF, Marchetti AA, Krantz K: The correction of stress incontinence by simple vesico-urethral suspension. Surg Gynecol Obstet 1949;88:509

[13] Burch JC: Urethrovaginal fixation to Cooper's ligament for correction of stress incontinence, cystocele, and prolapse. Am J Obstet Gynecol. 1961;81:281

[14] Wu JY. Surgical therapies of female stress urinary incontinence: experience in 228 cases. Int Urogynecol J. 2010;21:645

[15] Kjoldehe P. Long-term efficacy of Burch colposuspension: a 14-year follow-up study. Acta Obstet Gynecol Scand. 2005;84:767

[16] Alcalay M, et al, Burch colposuspension: a 10-20 year follow-up. Br J Obstet Gynaecol. 1995;102:740

[17] Demirci F, et al. Long-term results of Burch colposuspension. Gynecol Obstet Invest. 2001;51(4):243

[18] Pereyra AJ. A simplified surgical procedure for the correction of stress incontinence in women. Wet J Surg. 1959;65:223

[19] Giordano D. Guerison par autoplastie musculo-nerveuse d'une incontinence vesicale, suite de "befida spina'. Cong Frac de Chir. 1907;28:84

[20] Goebell R. Zur operative Beseitigung der angeborenen Incontinentia vesicae. A gynak Urol. 1910;2:187

[21] Frangenheim P. Zur operative Gehandlung der Inkontinenz der mannlichen Harnrohre. Verh dtsch Ges Chir. 1914;43:149
[22] Stoeckel W. Uber die Verwendung der Musculi pyramidalis bei der operative Behandlung der Incontinentia urinae. Zentralbl Gynak. 1917;41:11
[23] Price PB. Plastic operations for incontinence of urine and feces. Arch Surg. 1933;26:1043
[24] Aldridge AA. Transplantation of fascia for relief of urinary stress incontinence. Am J Obstet Gynecol. 1942;44:398
[25] McGuire EJ, Lytton B. Pubovaginal sling procedure for stress incontinence. J Urol. 1978;119(1):82
[26] Richter HE, et al. Patient related factors associated with long-term urinary continence after Burch coposuspension and pubovaginal fascial sling surgeries, Urology. 2010;
[27] Petros PE, Ulmsten U. An Integral Theory of femal urinary incontinence. Acta Obstetricia et Gynecologica Scandinavica. 1990;69:1
[28] Ogah J, et al. Minimally invasive synthetic suburethal sling operations for stress urinary incontinence in women. Cochrane Database of Systematic Reviews. 2009, Issue 4
[29] Falconer C, et al. Influence of different sling material on connective tissue metabolism in stress urinary incontinence women. Int Urogynecol J Pelvic Floor Dysfunct. 2001;12(2):19
[30] Tong A, Lin L, et al. In vivo tension sustained by fascial sling in pubovaginal sling surgery for femal stress urinary incontinence. Urology 2005
[31] Ulsten U, et al. An ambulatory surgical procedure under local anesthesia for treatment of female urinary incontinence. Int Urogynecol J. 1996;7:81
[32] Ulmsten U. A multicenter study of Tension-free Vaginal Tape (TVT) for the surgical treatment of stress urinary incontinence. Int Urogynecol J. 1998;9:210
[33] Ward K, Hilton P. Tension-free vaginal tape versus colposuspension for primary urodynamic stress incontinence: 5-year follow up. BJOG 2008;115:226
[34] Ogah J, et al. Minimally invasive synthetic suburethral sling operations for stress urinary incontinence in women. Cochrane Database of Systematic Reviews. 2009, Issue 4.
[35] Lapitan MC, Cody JD. Open retropuic colposuspension for urinary incontinence in women. Cochrane Database Systematic Reviews. 2012 June 13
[36] Novara G, et al. Updated systematic review and meta-analysis of the comparative data on colposuspension, pubovaginal slings and midurethral tapes in the surgical treatment of female stress urinary incontinence. Eur Urol. 2010;58(2):218
[37] Richter HE, et al. Retropubic versus transobturator midurethral slings for stress incontinence. N Engl J Med. 2010;362(22):2066
[38] Albo ME, et al. Treatment success of retropubic and transobturator mid urethral slings at 24 months. J Urol. 2012;188(6):2281
[39] Kenton K. 5-year longitudinal followup after retropubic and transobturator mid urethral slings. J Urol. 2015;193(1):203
[40] Position statement on restriction of surgical options for pelvic floor disorders. American Urogynecologic Society, 2013
[41] Position statement on mesh midurethral slings for SUI. SUFU, 2014
[42] Considerations about surgical mesh for SUI. FDA, 2013